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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/986,606	12/08/1997	NATHAN H. SLAONE	21578-013RCE	5146

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MINTZ, LEVIN, COHN, FERRIS, GLOVSKY
AND POPEO, P.C.
ONE FINANCIAL CENTER
BOSTON, MA 02111

EXAMINER	
LUKTON, DAVID	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 10/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/986,606	SLAONE, NATHAN H.	
	Examiner	Art Unit	
	David Lukton	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-6,8,9,15,17 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *4 and 17* is/are allowed.

6)☒ Claim(s) *5,6,8,15 and 18* is/are rejected.

7)☒ Claim(s) *9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pursuant to the directives of the amendment filed 7/2/04, claims 4-6, 8, 15, 17, 18 have been amended and claims 7 and 16 cancelled. Claims 4-6, 8, 9, 15, 17, 18 are pending.

Applicants' arguments filed 7/2/04 have been considered and found persuasive in part. Claims 4 and 17 are characterized as allowable at the present time; claim 9 is objected to because of its dependence on a rejected claim.

✧

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5, 6, 8, 15 and 18 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 8 and 18 are drawn to a method of killing a tumor cell. These claims encompass killing both *in vitro* and *in vivo*. However, enablement is lacking, at least for the case of achieving the "contacting" by administering the peptide to a tumor-bearing mammal.

As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988), the factors to consider in evaluating the need (or absence of need) for

"undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims. The following references discuss the matter of various attempts by oncologists to treat cancer: Viallet (*Lung Cancer* **15** (3) 367-73, 1996); Kemeny (*Seminars in Oncology* **21** (4 Suppl 7) 67-75, 1994); Newton (*Expert Opinion on Investigational Drugs* **9** (12) 2815-29, 2000); Giese (*Journal of Cancer Research and Clinical Oncology* **127** (4) 217-25, 2001); Garattini (*European Journal of Cancer* **37** Suppl 8 S128-47, 2001); Ragnhammar (*Acta Oncologica* **40** (2-3) 282-308, 2001).

As is evident, attempts to kill cancer cells in tumor-bearing mammals using agents which have exhibited *in vitro* activity leads to "unpredictable" results. In addition, applicant has made an admission (page 5, lines 1-2) that the peptide failed to kill tumor cells when SDS was absent.

In addition to the foregoing, there is another issue, which is that, even if applicants can demonstrate killing (*in vitro* or *in vivo*) of breast cancer cells, it will not follow that any and all tumor cells will be "killed" by the claimed peptide. The term "cancer" or "tumor" encompasses a wide variety of proliferative diseases, such as the following: prostate cancer, lung cancer, colon cancer, rectal cancer, bladder cancer, Non-Hodgkin Lymphoma,

melanomas of the skin, cancer of the Kidney and Renal Pelvis, pancreatic cancer, oral cancer, esophagal cancer, ovarian cancer, thyroid cancer, stomach cancer, brain cancer, multiple myeloma, liver and intrahepatic bile duct cancer, acute myeloid leukemia, chronic lymphocytic leukemia, Hodgkin's Lymphoma, testicular cancer, intestinal cancer, chronic myeloid leukemia, acute lymphocytic leukemia, cancer of the vulva, gallbladder cancer, malignant mesothelioma, bone cancer, joint cancer, cancer of the hypopharynx, cancer of the eye, cancer of the nose, cancer of the ureter, cancer of the peritoneum, gastrointestinal carcinoid tumors, bladder cancer, melanoma, breast cancer, non-hodgkin's lymphoma, ovarian cancer, endometrial cancer, pancreatic cancer, kidney cancer (renal cell), prostate cancer, leukemia, non-melanoma cancer of the skin. Also included are sarcomas and carcinomas, such as the following: fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinoma, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilms' tumor, cervical cancer, testicular tumor, lung carcinoma, small cell lung

carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, melanoma, neuroblastoma, retinoblastoma, leukemia, lymphoma, multiple myeloma, Waldenströom's macroglobulinemia, and heavy chain disease. There is no evidence of record that there exists any one agent that is effective against all of these cancer types, or most of them. The skilled oncologist would not regard it as realistic that one can extrapolate from a showing of inhibition of growth of one cancer cell type to inhibition of growth of all cancer cell types.

In addition to the foregoing, there is a closely related issue, which is that each of claims 5, 6, 8, 15 and 18 asserts that the claimed peptide will induce apoptosis of any tumor cell type. As it happens, the skilled artisan cannot predict what cell types will undergo enhanced apoptosis in the presence of a given compound "X". For example, Fang X. (*Biochemical Journal* **352 Pt 1** 135-43, 2000) discloses that lysophosphatidic acid inhibits apoptosis in fibroblasts; at the same time, Steiner M. R. (*Annals of the New York Academy of Sciences* **905** 132-41, 2000) discloses that lysophosphatidic acid induces apoptosis in neuronal cells. Thus, if a determination is made that a given compound will inhibit apoptosis of a given cell type, the skilled artisan cannot predict the cell types in which apoptosis will be inhibited, and the cell types in which apoptosis will be induced. This conclusion is reinforced by the findings of Tsuchiyama Y (*Kidney International* **58** (5)

1941-52, 2000) who discloses that while dexamethasone induces apoptosis in both CD8+ cells and CD4+ cells, Galectin-9 induces apoptosis in CD8+ cells, but fails to induce apoptosis in CD4+ cells. None of the foregoing references (i.e., Fang, Steiner, or Tsuchiyama) discusses apoptosis of tumor cells *per se*. However, if one cannot predict which (healthy) cells will undergo apoptosis, it stands to reason that one cannot predict which unhealthy cells will indergo apoptosis.

Applicants have submitted a declaration (filed 9/4/03) which purports to show that a peptide designated "PepA" is effective to reduce growth of cervical cancer cells in mice. However, this peptide ("PepA") is never identified specifically. What is stated in the declaration is that the peptide designated "PepA" "contains the amino acid sequence of SEQ ID NO:1". This is interpreted to mean that "PepA" is actually different from the peptide of SEQ ID NO: 1. Perhaps "PepA" has 10 more amino acids than the peptide of SEQ ID NO: 1. Or perhaps it contains 30 more. One can only speculate. But if one shows that a given peptide can exhibit a given pharmacological activity, one cannot "predict" that smaller peptides will exhibit the same activity. More often than not, activity is lost upon truncation.

Thus, all that has been shown is that the claimed peptide, when in the presence of SDS and in a petri dish (i.e., *in vitro*) will inhibit growth of breast cancer cells. From this applicants are extrapolating to apoptosis of any and all tumor cells *in vitro*, apoptosis of any

and all tumor cells *in vivo*, "killing" of any and all tumor cells *in vitro*, and "killing" of any and all tumor cells *in vivo*. And in addition to this, most of the claims do not require or suggest the presence of SDS.

Accordingly, "undue experimentation" would be required to practice the claimed invention.

*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached at 571-272-0925. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

D. Lukton

DAVID LUKTON
PATENT EXAMINER
GROUP 1600